

(FILE 'USPAT' ENTERED AT 13:54:26 ON 18 JAN 1999)

L1 19 KERATINOCYT? (5A) CLONAL

L2 139 (MEDIUM OR MEDIA) (5A) TOPICAL?

L3 516 (CULTURE (W) (MEDIA OR MEDIUM)) (P) (PHARMACEUT? OR TOPICAL? O

R C

L4 129 (CULTURE (W) (MEDIA OR MEDIUM)) (10A) (PHARMACEUT? OR TOPICAL?

OR

L5 124 L4 NOT L2

L6 8 ((SERUM FREE) (5A) (MEDIA OR MEDIUM)) (P) (WOUND? (5A) HEAL?)

(FILE 'HOME' ENTERED AT 14:42:40 ON 18 JAN 1999)

FILE 'BIOSIS, CAPLUS, MEDLINE, WPIDS' ENTERED AT 14:43:05 ON 18 JAN
1999

L1 196 ((SERUM FREE) (5A) (MEDIA OR MEDIUM)) AND (WOUND? (5A) HEAL?)
L2 124 DUPLICATE REMOVE L1 (72 DUPLICATES REMOVED)
L3 9 ((SERUM FREE) (5A) (MEDIA OR MEDIUM)) (10A) (TOPICAL? OR PHAR
L4 7 DUPLICATE REMOVE L3 (2 DUPLICATES REMOVED)

81. 5,371,089, Dec. 6, 1994, Method and composition for ameliorating the adverse effects of aging; Suresh I. S. Rattan, 514/261, 266, 844 [IMAGE AVAILABLE]

US PAT NO: 5,371,089 [IMAGE AVAILABLE]

L5: 81 of 124

ABSTRACT:

Compositions and methods are provided for countering the adverse effects of aging on cells in culture and *in vivo* in which cells are contacted with the compositions that ameliorate the adverse effects of aging on mammalian cells by slowing or reversing the changes that normally accompany aging of such cells but do not significantly increase the growth rate or total proliferative capacity of such cells. The compositions contain one or more 6-(substituted amino)purine cytokinins and preferably do not contain ingredients that promote cell division or that induce or potentiate the ability of the 6-(substituted amino) purine cytokinins to promote cell division.

Among the preferred applications of the compositions and methods provided herein are the preservation of or restoration of the health of mammalian cells in culture and, by application of the compositions to human skin, t

4. 5,591,709, Jan. 7, 1997, Compositions and methods for treating wounds; Ella Lindenbaum, 514/4; 424/484, 486, 487, 488; 514/3, 12, 21, 567 [IMAGE AVAILABLE]

US PAT NO: 5,591,709 [IMAGE AVAILABLE]

L6: 4 of 8

ABSTRACT:

The present invention relates to wound treatment formulations and methods for treating wounds utilizing these formulations. The formulations according to the present invention are useful for treating wounds by accelerating wound healing. These formulations generally comprise an effective amount of a non-steroidal anabolic hormone such as insulin, growth hormone, triiodothyronine, thyroxine or mixtures thereof, in combination with a cellular nutrient medium, preferably MCDB 153.

2. 5,681,561, Oct. 28, 1997, Compositions and methods for improving autologous fat grafting; Bernard Hirshowitz, et al., 424/93.7, 574; 514/2, 21 [IMAGE AVAILABLE]

US PAT NO: 5,681,561 [IMAGE AVAILABLE]

L6: 2 of 8

ABSTRACT:

The present invention relates to compositions and methods for enhancing the success of autologous fat grafting in a patient. The compositions according to the present invention are useful for enhancing autologous fat grafting by improving the survival rate of lipocytes which are injected into a patient as part of a fat grafting procedure. These compositions comprise a fat grafting effective amount of autologous lipocytes in combination with a lipocyte growth effective amount of a non-steroidal anabolic hormone selected from insulin, triiodothyronine/thyroxine (T₃ or T₄), mixtures thereof, and optionally, growth hormone, most preferably a mixture of all three hormones because of the favorable effect these three hormones exhibit in combination to promote autologous fat grafting, the hormones being further combined with a lipocyte growth effective amount of a nutrient medium, preferably a serum free nutrient medium as at least a minimum essential medium.

serum-free cell culture medium was supplemented with non-steroidal anabolic hormones, growth hormone, thyroxin and insulin, transferrin and sodium selenite. The medium was prepared in a 1 per cent alginate gel matrix. Under general anaesthesia with ketamine (Imalgene 1000, Rhone Merieux, France) four 2 times 2 cm full-thickness skin patches were surgically extirpated from the dorsum of Hartley-derived guinea-pigs. Each experimental group consisted of seven animals, i.e. 28 wounds that received the same treatment. Compositions of gelatin in saline, agarose in saline, agarose in medium and agarose in saline supplemented with the three hormones were compared to agarose in medium supplemented with the three hormones. After application of the gel (1 ml/cm²), the wounds were dressed with gauze, elastic adhesive bandage and netting. Change of bandage and administration of gel were performed every 48 h under general anaesthesia, at which time all the wounds were washed with warm saline, measured, photographed and redressed as above. Computerized morphometric measurements of the photographs of each wound, in sequence, were made using ImageMeasure software. The dynamics of wound closure were quantified, analysed and plotted. The agarose in medium supplemented with the three anabolic hormones induce statistically significant ($P < 0.001$) acceleration of wound closure when compared to controls. No statistically significant difference was found among the controls.

L2 ANSWER 54 OF 124 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 23
 AN 1993:240954 CAPLUS
 DN 118:240954
 TI Compositions and methods for treating wounds
 IN Lindenbaum, Ella
 PA Life Medical Sciences, Inc., USA
 SO PCT Int. Appl., 46 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 9304691 | A1 | 19930318 | WO 92-US7341 | 19920828 |
| | W: AT, AU, BB, BG, BR, CA, CH, CS, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, PL, RO, RU, SD, SE | | | | |
| | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG | | | | |
| | HU 67319 | A2 | 19950328 | HU 94-593 | 19920228 |
| | AU 9225879 | A1 | 19930405 | AU 92-25879 | 19920828 |
| | AU 670413 | B2 | 19960718 | | |
| | BR 9206433 | A | 19940927 | BR 92-6433 | 19920828 |
| | JP 06510453 | T2 | 19941124 | JP 92-505336 | 19920828 |
| | NO 9400406 | A | 19940328 | NO 94-406 | 19940208 |
| PRAI | US 91-752849 | | 19910830 | | |
| | WO 92-US7341 | | 19920828 | | |
| AB | The formulations of the invention are useful for treating wounds by accelerating wound healing. | | | | |
| | The formulations comprise an effective amt. of a cellular growth-stimulating compd. (growth hormone, insulin, transforming growth factor, epithelial growth factor, etc.) (concn. ≥ 0.05 ng/mL) in a (serum-free) cellular nutrient medium. Thus, a lyophilized powder of MCDB 153 medium was reconstituted with distd., sterilized water and supplemented with human growth hormone to a final concn. of approx. 0.5-2 ng/mL; in certain formulations, an amt. of insulin-transferrin was added to a final concn. of approx. 200 ng/mL. In some instances, approx. 1 wt.% gelatin or collagen was added to provide a gel product for delivery. The formulation was used to treat e.g. a patient having a heel decubitus-pressure wound. Modified serum- | | | | |

free culture medium supplemented with nonsteroidal anabolic hormone was tested for wound healing activity in animal studies.

L2 ANSWER 33 OF 124 CAPLUS COPYRIGHT 1999 ACS DUPLICATE 13
AN 1995:958515 CAPLUS

DN 123:350357

TI **Wound healing** compositions containing cell culture medium and growth hormones

IN Lindenbaum, Ella

PA Life Medical Science, Inc., USA

SO U.S., 9 pp.

CODEN: USXXAM

DT Patent

LA English

FAN. CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|--------------|------|----------|-----------------|----------|
| PI | US 5461030 | A | 19951024 | US 93-158808 | 19931129 |
| | US 5591709 | A | 19970107 | US 95-374944 | 19950118 |
| PRAI | IL 91-97127 | | 19910201 | | |
| | US 91-752849 | | 19910830 | | |
| | US 92-937486 | | 19920828 | | |
| | US 93-25216 | | 19930302 | | |
| | US 93-158808 | | 19931129 | | |

AB The title formulations are useful for treating **wounds** by accelerating **wound healing**. These formulations comprise an effective amt. of a **serum free** cellular nutrient **medium** in combination with an effective amt. of at least one cellular growth stimulating compd., e.g. a natural anabolic hormone or transforming growth factor. Thus, 100 g of lyophilized powder of MCDB 153 culture medium was reconstituted with water and supplemented with human growth hormone to final concn. of 0.5-2 ng/mL. In certain formulations insulin-transferrin was added to final concn. of 5.μg/mL and collagen or gelatin at 4% concn. The compns. were effective in treatment of pressure wound and skin ulcers.

L2 ANSWER 42 OF 124 BIOSIS COPYRIGHT 1999 BIOSIS DUPLICATE 16
AN 1995:181969 BIOSIS

DN PREV199598196269

TI **Serum-free** cell culture **medium** induces acceleration of **wound healing** in guinea-pigs.

AU Lindenbaum, E. S. (1); Tendler, M.; Beach, D.

CS (1) Fac. Med., Technion, POB 9649 Haifa Israel

SO Burns, (1995) Vol. 21, No. 2, pp. 110-115.

ISSN: 0305-4179.

DT Article

LA English

AB Among the current methods employed in the treatment of wounds, a moist dressing is considered to be the optimal environment for the process of **healing** thereby avoiding desiccation of the **wound bed**. This study is based on the hypothesis that wound cell proliferation is dependent not only on moisture but also upon the composition of the moist microenvironment in the wound. That composition in turn is formed by diffusion of nutrients from the existing vascular bed in and around the wound as well as by the wound cells' cellular products. Since in wounds the impaired vascular supply causes tissue deprivation, a continuous supply of nutrients and hormones will create an optimal substrate for cellular mitogenic activity, synthesis of matrix, growth factors and cytokines leading to **wound healing**. Modified

123. 4,385,049, May 24, 1983, Stable high internal phase ratio topical emulsions; Robert C. Cuca, 514/786, 777, 784, 785, 939, 941 [IMAGE AVAILABLE]

US PAT NO: 4,385,049 [IMAGE AVAILABLE]

L2: 123 of 139

ABSTRACT:

Delivery systems for topical preparations which are commercially stable. The emulsions are water-in-oil in which the water phase comprises at least 75% of the emulsion by volume. The emulsifier is a nonionic oil soluble straight or branched chain ester or combination thereof composition having at least two hydrogen bonding sites per molecule.

1. 5,834,312, Nov. 10, 1998, Process and media for the growth of human epithelia; John J. Wille, Jr., 435/405, 325, 383, 384, 404 [IMAGE AVAILABLE]
2. 5,814,511, Sep. 29, 1998, Human breast epithelial cell type with stem cell and luminal epithelial cell characteristics; Chia-Cheng Chang, et al., 435/371, 378, 380, 387, 405, 406 [IMAGE AVAILABLE]
3. 5,795,781, Aug. 18, 1998, Cell competency solution for use in the formation of a histologically-complete, living, human skin substitute; John Jacob Wille, Jr., 435/404, 383; 623/15 [IMAGE AVAILABLE]
4. 5,741,642, Apr. 21, 1998, Assay for detecting the expression of a gene encoding human keratinocyte growth factor (KGF); Jeffrey S. Rubin, et al., 435/6, 91.2; 536/23.1, 24.3, 24.33 [IMAGE AVAILABLE]
5. 5,731,170, Mar. 24, 1998, DNA encoding a growth factor specific for epithelial cells; Jeffrey S. Rubin, et al., 435/69.4, 69.7, 71.1, 252.3, 252.8, 254.2, 320.1, 358, 365; 536/23.4, 23.51 [IMAGE AVAILABLE]
6. 5,728,377, Mar. 17, 1998, Methods and compositions incorporating IP-10; Andreas H. Sarris, et al., 424/85.1; 435/69.5; 530/351 [IMAGE AVAILABLE]
7. 5,707,805, Jan. 13, 1998, Assay for detecting keratinocyte growth factor (KGF) and its activity; Jeffrey S. Rubin, et al., 435/6, 7.1, 7.21 [IMAGE AVAILABLE]
8. 5,686,307, Nov. 11, 1997, Serum free medium for use in the formation of a histologically complete living human skin substitute; John Jacob Wille, Jr., 435/405, 383, 384, 404 [IMAGE AVAILABLE]
9. 5,686,116, Nov. 11, 1997, Methods of enhancing repair, healing and augmentation of bone implants; Richard Bockman, et al., 424/650; 514/8, 492 [IMAGE AVAILABLE]
10. 5,665,870, Sep. 9, 1997, Method of purifying keratinocyte growth factor (KGF); Jeffrey S. Rubin, et al., 530/412, 399, 417; 930/10 [IMAGE AVAILABLE]
11. 5,654,405, Aug. 5, 1997, Antibodies to human keratinocyte growth factor (KGF) and related pharmaceuticals; Jeffrey S. Rubin, et al., 530/387.9; 424/139.1, 141.1, 145.1; 435/336; 530/388.24, 389.2 [IMAGE AVAILABLE]
12. 5,650,317, Jul. 22, 1997, Human breast epithelial cell type with stem cell and luminal epithelial cell characteristics; Chia-Cheng Chang, et al., 435/371, 378 [IMAGE AVAILABLE]
13. 5,583,102, Dec. 10, 1996, Human thrombomodulin in wound healing; Steven R. Lentz, et al., 514/8, 12, 21; 530/350 [IMAGE AVAILABLE]
14. 5,364,785, Nov. 15, 1994, Method of isolating lung cell line; Jennie P. Mather, et al., 435/378, 4, 6, 29, 32, 70.1, 391 [IMAGE AVAILABLE]
15. 5,292,655, Mar. 8, 1994, Method for the formation of a histologically-complete skin substitute; John J. Wille, Jr., 435/384, 387; 623/15 [IMAGE AVAILABLE]

16. 5,262,298, Nov. 1993, Method to assess the ability of a substance to inhibit or stimulate keratinocyte autocrine factor production; Gary D. Shipley, et al., 435/6, 29; 436/63 [IMAGE AVAILABLE]

17. 4,940,666, Jul. 10, 1990, Process and defined medium for growth of human epidermal keratinocyte cells; Stephen T. Boyce, et al., 435/371, 405, 406, 408 [IMAGE AVAILABLE]

18. 4,673,649, Jun. 16, 1987, Process and defined medium for growth of human epidermal keratinocyte cells; Steven T. Boyce, et al., 435/378, 384, 387, 391, 405, 406, 408 [IMAGE AVAILABLE]

19. 4,016,036, Apr. 5, 1977, Process for serially culturing keratinocytes; Howard Green, et al., 435/347; 424/85.1; 435/173.1, 373, 391 [IMAGE AVAILABLE]